Issue #02 November 2015

Amsterdam Science

Green Computer Networks

Reparing the retina by gene therapy

Piet Borst, a life full of science

First time lucky?

The response to the first edition of Amsterdam Science was overwhelming! Many of our colleagues congratulated us with the content of the magazine and the nice "look and feel" of the printed version. The magazine landed on the reading tables of research institutes, but also in hotel lobbies, Ministries, the Amsterdam municipality office, Brussels and many other unexpected places. Our mission to make the first edition of Amsterdam Science visible was a great success. To our surprise, even the response to the puzzle was almost instantaneous and we received very elaborate solutions, including in the form of a computer script that could be used to solve the riddle. Let's see how the new puzzle is received.

Not just the paper version, but also the website received compliments and was visited frequently in the first weeks of its existence online. Of course, although a great start, Amsterdam Science #1 was not perfect and we received very useful feedback on both the magazine and the accompanying website.

As you can see in Amsterdam Science #2, this has resulted in format changes for the magazine: the page size is slightly larger to accommodate a larger font and boost the size of the images, both measures aiming at making reading more relaxed and comfortable. On the website we worked on the online submission form and have clarified our selection criteria for contributions. This led to more submissions made directly to the magazine, meaning that the second issue not only covers all disciplines, but also contains contributions from institutes other than the two universities who initiated the Amsterdam Science project.

Further expansion in the circle of contributing institutes is an explicit goal for the next issues, and inviting and recruiting more partners to the editorial board from outside the UvA or VU is a key step on this path. New board members are needed as, after enthusiastic and much-valued service, Monalisa, Dorota, Jeroen and Anne are stepping down in the closing stages of their PhD project or Master study. Also on behalf of our readers, we sincerely thank them for their inspiring contributions and wish them well with their careers.

On the cover and on the centrefold you will find amazing images and with the help of all contributing authors we can bring you a kaleidoscopic overview of what Amsterdam Science has to offer. Enjoy the second issue, one that we feel proves that the magazine's winning streak is more than a case of first time lucky!

On behalf of the Editors-in-Chief,
Michel Haring

ABOUT THE COVER IMAGE:
Hubble telescope image of the star cluster 'Westerlund 2'. This cluster harbours some of the hottest, brightest and most massive stars in our Galaxy, which illuminate the remainders of the clouds of gas and dust out of which they were formed. More information on page 4.

Image credit: NASA, ESA, the Hubble Heritage Team (STScI/AURA), A. Nota (ESA/STScI), and the Westerlund 2 Science Team.

& more

colophon

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On the cover

Hubble's 25th birthday

→ The spectacular images taken by the Hubble Space Telescope have fascinated two generations of professional astronomers and the general public alike. Hubble is celebrating its 25th birthday, which is truly exceptional for a space-based observatory, and is still going strong. Astronomy researchers still fiercely compete to get observation time using Hubble. How else could NASA and ESA celebrate this event than by releasing another spectacular image (and even a fly-through movie) of the enigmatic star cluster 'Westerlund 2' (see magazine cover)? This star cluster harbours some of the hottest, brightest, and most massive stars in our Galaxy, illuminating the remainders of the clouds of gas and dust out of which they were formed. UvA astrophysicist Selma de Mink, a newly hired assistant professor and MacGillavry Fellow at the Anton Pannekoek Institute, is one the scientists who proposed this observing programme using Hubble. Together with her students and colleagues she combines theoretical models and the exquisite data taken by the Hubble Space Telescope to better understand these extreme stars.

"Massive stars are very rare and live very short lives," explains De Mink, "at least in comparison to ordinary stars such as our own Sun. On top of that they tend to hide in very dense regions obscured by gas and dust. This makes it very challenging to study them. The star cluster Westerlund 2 is one of the rare places where we can study massive stars."

Although massive stars are vastly outnumbered, they play many premier roles in astrophysics. The very first stars that formed in the Universe after the Big Bang where thought to be very massive. The Universe was still dark and filled with neutral hydrogen. The hot radiation from the first massive stars ionized this gas, making the Universe transparent again, bringing an end to the cosmic dark ages. Since then, multiple generations of massive stars fused the primordial hydrogen into heavier elements, such as the oxygen that now allows us to breath. Understanding how massive stars live their life is a small but crucial step in understanding our own cosmic history.

Hubble has been crucial for our understanding of how massive stars live their lives. Taking images from space, Hubble can gather data in wavelength regions blocked by Earth's atmosphere, such as the ultraviolet, where hot, massive stars emit most of their light. Furthermore, Hubble takes data in the near-infrared region, which allows us to see through the dusty gas clouds that typically surround them. Above all, the superb spatial resolution allows us to zoom in on the densest regions of clusters, where massive stars are born.

An interview with SELMA DE MINK, Assistant Professor, MacGillavry and Marie Curie Fellow at the Anton Pannekoek Institute of the UvA.

© autors: SARAH BRANDS, Master's student in Astronomy & Astrophysics of the UvA, and MARK GOLDEN, Professor of Condensed Matter Physics at the Institute of Physics of the UvA.

"The near-infrared data of Hubble allow us to see through the dusty gas clouds that typically surround stars."

← Figure
Hubble owes its long life to several servicing missions during which astronauts from the space shuttle risked their lives to install new cameras and instruments, and replace broken parts. This picture was taken just after space shuttle Atlantis captured Hubble with its robotic arm on 13 May 2009, marking the start of a mission to upgrade and repair the telescope. © NASA.

The most striking part of the cover image is the dusty cloud visible on the lower left: when looking closely one can distinguish pillars of dust, which are places where lower-mass stars similar to our Sun are being formed. The ionising radiation of the massive stars of the central cluster is eroding these dusty pillars, giving them their spectacular shapes.

The cluster itself is visible in the centre of the image as a dense clump of stars that appear to be red. In reality the stars are extremely blue and hot, shining most of their radiation in the ultraviolet. The stars appear red because their light passed through many layers of gas and dust before it reaches the earth. The blue stars that you can see in the image are in the foreground and are much closer to Hubble. The Westerlund 2 cluster itself is located roughly 20,000 light-years away.

"After so many years of service, Hubble is still one of the most productive and highly oversubscribed astronomical observational facilities. But for how long? The telescope hopefully has a few years to go, but its instruments are degrading quickly as they face harsh conditions in space. One scenario is that one of its gyroscopes will fail first. These are crucial in pointing the telescope at the distant targets and keeping it stable. Also its very sensitive UV spectrograph, crucial for understanding massive stars, has got to be in bad shape. NASA hopes to launch its infrared successor, the James Webb Telescope, in a few years. But for the real successor of Hubble we have to wait for the telescope envisioned as the new NASA flagship mission of the 2025 – 2035 period, christened with the fitting acronym ATLAST." Ω

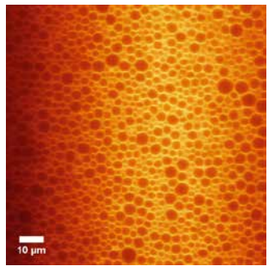
Traffic jams on the micro-scale

© MAUREEN DINKGREVE performed this research while a MSc student in the Soft Matter group at the Institute of Physics of the UvA, where she is now a PhD student.

→ Traffic jams are a common phenomenon on highways; with too many cars on the road, traffic gets stuck. On a microscopic scale, such jamming also occurs in materials such as emulsions, foams and suspensions if there are too many particles or drops per unit volume. Consequently, everyday materials such as beauty creams and toothpaste can be jammed as well. In the jammed state the materials are solid-like but can be made to flow if a large enough force is applied. Toothpaste, for instance, behaves like a solid on your toothbrush (it doesn't change shape under the gravitational force) but can be squeezed out of the toothpaste tube, flowing like a liquid.

Understanding and predicting this jamming transition from solid-like to fluid as a function of system parameters is a subject of considerable fundamental and industrial interest. Recently, jamming has been considered as a new kind of phase transition, similar to the classical phase transitions we know between solid, liquid and gas phases. The latter can be described in a universal way, in the sense that the melting of ice follows similar rules as the melting of iron.
We studied the flow behaviour of four different jammed systems: two types of emulsions, a foam and a polymer gel. We showed that the jamming transition from flow to no flow happens in a universal way here as well. This allowed us to develop a model for the microscopic dynamics that describes the rearrangements of the particles or bubbles with respect to each other, and agrees with the experimental data. This is the first time that the flow behaviour of four completely different materials were described with a single, universal model, which brings us one step closer to truly understanding the jamming phenomenon. Ω

→ Reference
M. Dinkgreve, J. Paredes, M. A. J. Michels, and D. Bonn, Universal rescaling of flow curves for yield-stress fluids close to jamming. Phys. Rev. E 92, 012305 (2015).



↑ Figure
Confocal microscope image of a jammed emulsion. The high concentration of droplets inhibits their free movement, resulting in a solid-like flow behaviour.

Speedy human neurons outsmart mice

© GUILHERME TESTA-SILVA obtained his PhD at the Vrije Universiteit Amsterdam in the group of Huibert Mansvelder, from which this paper resulted. Currently he works as postdoc at the Australian National University in Canberra.

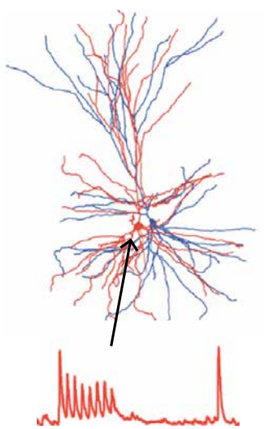
© HUIBERT MANSVELDER is Professor of Integrated Neurophysiology at the Neuroscience Campus Amsterdam of VU/VUmc.

→ Thinking, focusing, learning and remembering depend on cells or neurons in our brain communicating with each other. What we know about neuronal communication comes from research with laboratory animals (often mice). Up till now, it was simply assumed that human neurons would function in the same way as mouse neurons. By listening in on conversations between two neurons, researchers from the Vrije Universiteit Amsterdam (VU) and VU Medical Center (VUmc) found that human synapses, which are the contact points between neurons, are much more efficient than those in the mouse brain.

Human synapses have much better endurance and can continue transferring information over time scales at which mouse synapses are already exhausted. Human neurons can also detect much finer details in the electrical communication, which increases their information transfer. One can imagine this as mouse neurons communicating over a low-bandwidth telephone line, whereas human neurons are connected via a strong 4G connection.

So why has this experiment not been done before? The reason why we know so little about human neurons and how they function is that one has to work with living human brain tissue; all the neurons should be healthy and alive. But where do we get fresh human tissue? Our research is the result of collaboration between neurosurgeons and us as basic neuroscientists. During neurosurgical procedures to remove brain tumors and treat epilepsy, additional brain tissue sometimes has to be removed, for example to gain access to the relevant part of the brain. This tissue is perfectly suited for our research. To make this study possible, patients who have undergone neurosurgical treatment donated their tissue, which we used to study neuron communication. A next step will be to find out whether the faster neurons and synapses in our brain can explain why humans have so much more thinking power than other species with similar brain sizes. Ω

→ Reference
G. Testa-Silva, M.B. Verhoog, D. Linaro, C.P.J. de Kock, J.C. Baayen, R.M. Meredith, C.I. de Zeeuw, M. Giugliano, H.D. Mansvelder, High bandwidth synaptic communication and frequency tracking in human neocortex. *PLOS Biology* 12, e1002007 (2014).



↑ Figure
The synaptic connection between two human neurons (red, blue, scale bar 0.1 mm) can be observed by electrically stimulating the blue cell, after which the red cell responds with electrical activity.

An interview with Piet Borst, clinical biochemist, cancer researcher and former director of the Netherlands Cancer Institute

A life full of science

authors:
Michel Haring and
Sarah Brands, Amsterdam
Science editors

→ Organizing an interview with professor Piet Borst turns out to be easy: “Being a retired professor means that I have oceans of time, please come by!” When we arrive in the main Hall of the Antoni van Leeuwenhoek Hospital in Amsterdam-West, professor Borst himself comes to meet us: “People tend to get lost when they have to find their way to the laboratory, that is why I rather pick up my guests myself”. The interview takes place in his room in the Netherlands Cancer Institute. After he serves us a cup of coffee we quickly switch from professor to “Piet”, as he likes to keep things informal. And he likes to talk… So we need to guide him to our questions, otherwise he would bury us in anecdotes and science facts. Given that he is eighty-one and still active in scientific research we set out to discover the secret of his success.

How did you come to choose your research fields of biochemistry and molecular biology?

“It was just coincidence that brought me there! I never planned my career, everything happened by chance. Originally, I wanted to be a doctor and do clinical research. My father was a professor of internal medicine in Amsterdam, an excellent physician and researcher with an empathic attitude towards his patients. He was the ideal role model and this drove me towards a study in medicine. While I was waiting for a training position as medical doctor I had some time to kill and I decided to train myself in lab work and doing research. My father advised me to contact a young professor in Biochemistry at the University of Amsterdam: Bill Slater. I worked in his lab for four months and continued my studies in medicine afterwards, just as planned. However, a few months later, when I was doing the training internship for my medical studies I got a call from Slater: some doctor quit a research project and Slater wanted me to continue that work. But I was just in the middle of my medical training! It didn’t seem a good idea at first. Well, Slater convinced me to do it, and so I did. It turned out that I really liked doing the research, and so it happened that I completed my PhD thesis on metabolism of mitochondria (the energy generating organelles of the cell) in the lab of Bill Slater, while I simultaneously finished my study in medicine and became a physician.”

“Absolutely no job can compete with doing research.”

So in 1963 you were both a medical doctor and a researcher. What did you want to do next?

“I wanted to become an endocrinologist, a doctor specialized in hormones. There was a very good endocrinologist in Leiden, Querido, and I applied for a trainee position, but again the fact that there was a waiting list changed my career path. Through Slater I came in contact with a Nobel prize winner in America, Severo Ochoa, who worked on nucleic acids. For two years I lived in New York and studied the multiplication of bacterial

Born
1934, Amsterdam, The Netherlands

Study
1952-1963, Medicine [MD], with additional training in Biochemistry and Molecular Oncology

PhD
1961, Biochemistry, UvA

Work
1963-1964, biochemistry postdoc at New York University, United States

1964-1981, various research staff positions at the UvA

1983-1999, Research Director and later Chairman of the Board of Directors of the Netherlands Cancer Institute – Antoni van Leeuwenhoek hospital, Amsterdam
Since his retirement in 1999, staff member at NKI-AvL.

viruses in bacteria - something completely different from what I had done before. I learned a lot about nucleic acids and genetics. While I knew absolutely nothing about these subjects when I started, this knowledge later turned out to be extremely useful. At that time I was still preparing myself to work with Querido when I would return to the Netherlands, but once again things went different than planned: I got a call from Slater, who offered me a position as Associate Professor in Amsterdam. I was only 30 years old at that time, it was a great offer and I accepted it. Things went great with me and likewise with my biochemistry research: everything I did, resulted in something interesting. Luck was always on my side."

Do you really believe it was luck?
"Well, I probably do have a bit of talent, too. I discovered many things, more than most people have discovered, because almost everything I started resulted in something interesting. This was not just luck indeed - it's difficult to quantify, but I think it is mainly about two things. Firstly: being enormously diligent. To be a good researcher, you will need to have a certain intuition about what is interesting to investigate, and what's not. This intuition is based on a huge reservoir of knowledge, which you will have to gather first. Being diligent and working hard will help you with that. Secondly, I have an eye for experimental artefacts. If you lack this, you will waste a lot of time studying artefacts. Many biochemists spend a lot of time studying artefacts. I know a lot of people who are much smarter than I am and who work very accurately, but missed the common sense of realising 'this is just not the thing we're looking for'. If you do have this common sense, you have more time for discovering really interesting things."

But how do you discover interesting things? Students often want to know whether it is better to focus on one thing as soon as possible, or instead first learn a bit of everything and specialise later. What would be your advice?
"First of all, early on in your career the environment you work in is of utmost importance. The better the environment, the more chances you get to explore your potential. It's hard to build a castle in a swamp, so to say. To become a good biochemist, you have to start in a good lab, this is essential. Later, when you're more experienced, you can adapt a lab in a way you like, but in the beginning you are totally dependent on your environment: the supervision you get, the project you do, the quality of the work around you, your peer group. Secondly, for people who are doing good work and are ambitious, I think it is wise to get a broad basis. With this I do not mean knowing a little bit of everything, but instead diving deep into several different projects. For me, this worked out great. When I was 30 and started my own lab for the first time, I knew a lot about mitochondria as well as nucleic acids. The choice of my research field was therefore easy: a combination of the two. People were already studying this, but the people specialized in nucleic acids thought mitochondria were complicated! And the people specialized in the mitochondria thought the same about the nucleic acids. As an expert in both fields, however, I was in a unique position, and in less than a year I found something fascinating."

"Biologists have to deal with the unique differences between each organism, and the randomness of nature."

Piet Borst is a family man. In the middle of the interview his phone starts beeping: a Whatsapp message. "Sorry, but I have to check this, it's my granddaughter - yes, when you grow older your priorities change", he says when he sees how we wait for him to continue talking. He looks at his phone. "Great! My granddaughter wants to study medicine and she's been accepted at the university!". He laughs: "You probably think, that man always works, but you're wrong, I have a rich social life. Seven grandchildren and I see them all the time."

You talk about several things you have discovered. What discovery are you most proud of?
"As a PhD student I discovered a metabolic pathway: a new cycle in the human metabolism. Later, people have discovered that it was one of the main cycles: the malate-aspartate cycle for the oxidation of extra-mitochondrial NADH. For a while it was even called the 'Borst-cycle'. I am still proud of this discovery, because it was a combination of different things I had found before. Without each other they didn't make sense, but at a certain moment I could tie everything together and the puzzle was complete. That is the great thing about research, actually: for days, weeks, months you are puzzling, trying to figure things out, thinking 'how on earth is this possible?' and then, suddenly, everything falls into place."

Another interesting discovery was why it is so hard for the human body to fight trypanosoma, a parasite that can cause the fatal sleeping disease. What made you start this research?
"A group in Belgium studying the trypanosome parasites was looking for somebody specialised in the DNA present in their mitochondria. They asked me and I said yes. I had two drivers for joining them: First, I did not think that the people working on it were incredibly talented - arrogant, that was what I was back then, I lost that now - so I thought: if I start in this area with one PhD student I have a good chance to compete with the rest of the world. Second, it was a good thing that the research was relevant, in the sense that it directly contributed to solving health threats. Relevant, applied research, that was a thing that the students were looking for at that time."

So you think applied research is more relevant?
"No, that's not true! You should not underestimate the importance of fundamental research. If you do fundamental research, ultimately it will always lead to knowledge that can be applied in such a way that society can benefit from it. Sometimes people don't realise that all the big revolutions in for example technology and health care are the result of fundamental research, funded by governments. Such research maybe did not seem relevant at first - its purpose was just the gathering of knowledge - but then, suddenly, it turned out to be of great interest! Fundamental research is of utmost importance.

The budget for fundamental science is shrinking, which is really alarming. Partially this is due to the fact that applied science is more in the picture, but it is also a consequence of overall budget cuts. When the economic recession started, 600 million of the budget for science was cut. Now the economy gets better, but nobody says: shouldn't we replenish the science budget again? What is happening at the moment, could be described as a biological process called autophagy: just as a hungering cell eats itself, we are gradually consuming all the fundamental knowledge we built up in the past - in ten years we will be reaping the consequences. I am preparing a financial analysis of the 'topsector' policy to show how little money is being spent on fundamental research, to confront the managers and politicians with the consequences of their policy."

"Just as a hungering cell eats itself, we are gradually consuming all the fundamental knowledge we built up in the past....."

Was there ever a moment when you considered to stop doing research and instead switch completely to a management function? As a scientist you have been director of the Netherlands Cancer Institute for sixteen years.
"No, because absolutely no job can compete with doing research. It is different every day, always surprising. In all other areas, medicine, politics, all days are the same in the end. Actually, we are very privileged that we, scientists, can do research: never a dull day. You always have a goal, you are carrying out a journey to something new, a discovery, that is really special. When I became director of the Netherlands Cancer Institute I wanted to show that management by a peer works much better than management by so-called professionals. Being part of the organisation I could collect feedback from within the organisation much more efficiently. More organisations have adopted this approach, so it is clear that this approach works."

What has the era of genomics research delivered? Are there new developments that you would like to highlight?
"There are a number of developments in life science that will radically change medical practice. All the genetics and genomics tools that we have been developed in the past ten years will allow the development of personalised medicine, notably in cancer. It will also allow genetic testing for rare and dramatic genetic defects. If this can be tested already in the mother's blood during early pregnancy, parents will have the possibility to make a choice. Even more radical: new genome engineering technologies like CRISPR-CAS will make it possible to repair genetic defects in single cells, like fertilized human egg cells. You can imagine that this creates even more difficult ethical dilemmas. Should we not prevent dramatic genetic defects if we can? Just like the discussion we had about recombinant DNA technologies in the eighties, we will have to discuss with scientists, clinical geneticists and the public what opportunities and threats are associated with these new developments."

As we are wrapping up the interview Piet comes up with a statement about the differences between biology and astrophysics, because Sarah – one of the interviewers – is doing a Master's in this area.
"Physics works with 'laws'. Biology, however, works with evolution. The fun thing about evolution is, and this makes our area of research so fascinating but at the same time also very complicated, that it is based on mutations of genes. Mutations are random, so the consequence is that evolution is random! Subsequently the things that are useful, that do work, are selected: the things that are viable and competing. Once every twenty years, the university proposes to start a chair for theoretical biology, Then I laugh, because really, theoretical biology doesn't exist! While physicists, or even chemists, know that they can reproduce experiments in an exact manner - a pot of salt is the same everyday - biologists have to deal with the unique differences between each organism and the randomness of nature. Some people can't stand it, but we, biologists, love it. Ω

Self-learning search engines

©
ANNE SCHUTH
PhD student in the Information and Language Processing Systems group at the Informatics Institute, UvA.

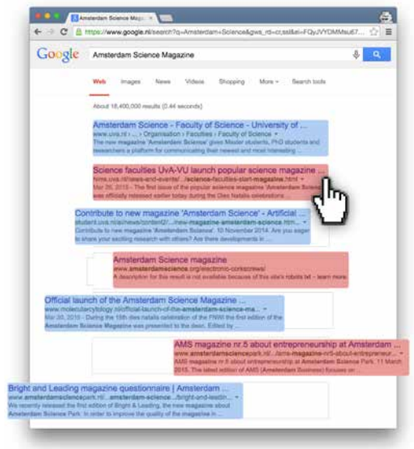
→ **How does a search engine such as Google know which search results to display? There are many competing algorithms that generate search results, but which one works best? We developed a new probabilistic method for quickly comparing large numbers of search algorithms by examining the results users click on. Our study was presented at SIGIR 2015, the leading international conference on information retrieval, held in Santiago (Chili) last summer.**

Interleaving
Developers of web search engines constantly create hundreds of alternative search algorithms, all of which aim to find the best possible match between a user's information need and web pages. It is vital for both the search engine and the user to know which of these algorithms produces the best results. A common way to compare search algorithms is through interleaving, a method whereby the search engine analyses the users' click behaviour to determine a preference between two alternative algorithms. After the user has typed in a query, the unique results of two search algorithms (blue and red in the Figure) are interleaved alternatingly (from top to bottom, and displayed to the user as a single list. If the user then clicks on a result found by one search algorithm (red), the algorithm analysis infers that in this particular case the algorithm generating the selected result produces better results than the other one. By scaling up this type of inference to cover millions of users, the search engine automatically learns which algorithms yield the best results.

Multileaving 1.0
Interleaving is, however, limited by the fact that only two algorithms can be compared at a time, and thousands of comparisons may therefore be required to determine which one of hundreds of existing algorithms really works the most effectively. So-called multileaving methods, which have been developed at the University of Amsterdam, allow multiple algorithms to be compared simultaneously. In earlier work, we did so by combining the results from many lists of results at once (in the example of blue and red lists, imagine also adding orange and green lists, etc.). The multileaved result list that is shown to the user is then a mix of results originating from many search algorithms - a multicoloured list. We keep track of where each of the results came from (their colour), and, as with interleaving, we observe which search algorithm (colour) attracts most clicks from users. Again, the search algorithm that receives most clicks wins. Typically, once this has been established, the search engine will completely switch over to the victorious search algorithm for all its users and queries.

Next step: probabilistic multileaving
Our newest method takes multileaving a step further. While we still combine the results from many search algorithms into a single multileaved result list, we now do so probabilistically. Instead of alternatingly picking results from each of the lists, always working from the top-ranked downwards, we now define a (high) probability that the top-ranked result is picked, leaving a non-zero probability that a lower ranked result is selected instead. By making the multileaved list probabilistic, we ensure that any combination of search algorithms (coloured lists) could have resulted in the multileaved list that is shown to a user. This has the major advantage that we can retrospectively evaluate any search algorithm, using a multileaved result list that has already been shown to a user. In other words, it now becomes possible to reuse old combinations of multileaved result lists and users' clicks to keep evaluating new search algorithms. As can be expected, the search algorithms that originally contributed results to the multileaved result list, or algorithms that are very similar, can be evaluated with higher confidence than very different search algorithms. However, even working at lower confidence levels, it is a major advantage of our probabilistic multileaving method that new search algorithms that were not even invented when the multileaving took place can be evaluated retrospectively. This way, our method can identify the best search algorithms much faster, enabling search engines such as Google to self-improve much more efficiently. Ω

"the 'users' click behaviour determines the preference for the search algorithm"



↑ **Figure**
An interleaved results list is generated by alternatingly selecting results from the results lists of two different algorithms (highlighted in red and blue).

Link to article:
http://bit.ly/probabilistic-multileave-pdf

→ **Reference**
A. Schuth, R.-J. Bruintjes, F. Büttner, J. van Doorn, C. Groenland, H. Oosterhuis, C.-N. Tran, B. Veeling, J. van der Velde, R. Wechsler, D. Woudenberg, M. de Rijke, Probabilistic Multileave for Online Retrieval Evaluation. *Proceedings of the 38th International ACM SIGIR Conference on Research and Development in Information Retrieval*, 955-958 (2015).

Hundred years ago

→ In the early 1900s, it was well known that the same fossils could be found in the rocks of different continents. At first, enormous land bridges were invoked to explain fossil evidence such as *Glossopteris*, a Permian fern of which fossils were found in Africa, South America and Australia. However, no trace of the land bridges was found. Alfred Wegener (1880 - 1930), professor in meteorology and geophysics, realised that the outline of the continents, 200 meters below present sea level, fitted together like the pieces of a giant jigsaw puzzle. 'The continents must have shifted,' Wegener wrote. 'South America must have lain alongside Africa and formed a unified block.' Before their separation, the continents were fused together in what he named the 'Urkontinent' – now known as Pangaea. 'The parts must have become increasingly separated over a period of millions of years,' Wegener wrote. He suggested that the 'Urkontinent' was pulled apart by the centrifugal force from the Earth's rotation and that the continents drifted apart with rates of up to 250 cm per year until reaching their current positions.

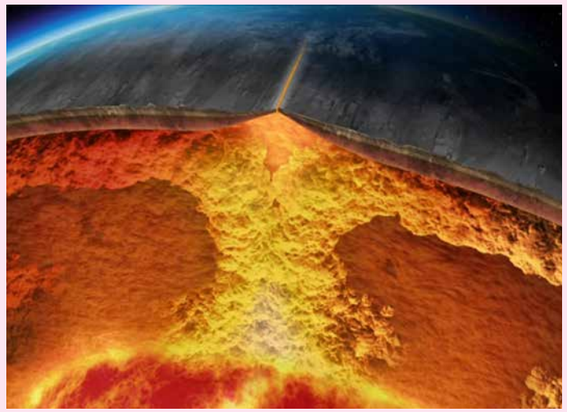
In 1915, Wegener published his theory in *Die Entstehung der Kontinente und Ozeane* (The Origin of Continents and Oceans), which was greeted with great scepticism. The mechanism involving centrifugal forces proved erroneous, and in the end it took until the 1970's for the theory of continental drift (plate tectonics) to be accepted. Mapping the topology of the ocean floor, the geologist Marie Tharp (1920 - 2006) discovered a chain of mountains splitting the large ocean basins in two. Tharp and the geologist Bruce Heezen (1924 - 1977) recognized that the mid-ocean ridges were lines along which the oceanic crust was splitting apart, pushing the continents away from each other.

Modern-day satellites equipped with GPS measure the rates of continental drift, which turn out to be up to 10 cm per year. The 80-km-thick continental crusts float on a dense mantle of molten rock, or magma. The magma flows up and down cyclically due to radioactive heating in the Earth's core. Magma flowing outwards from the mantle is diverted horizontally when it meets the crust, and this exerts extensional stress, pulling the crust apart in so-called rift zones. The Mid-Atlantic Ridge is a typical rift zone, and in these locations, volcanic eruptions continuously add magma to the diverting crust, pushing both sides apart, like slowly peeling apart two pieces of paper. By measuring the electromagnetic signal in the crust parallel to the ridge – imprinted by the Earth's electromagnetic field in magnetic minerals at the moment the magma cooled down to temperatures below 580°C – we can estimate when each portion of crust was added. The fact that the estimated age of the crust scales with its remoteness from the rift zone confirms the tectonic picture as being correct. Reconstructions suggest that it was around 300 million years ago when Wegener's 'Urkontinent' split.

Plate tectonics is still an active field of scientific inquiry in itself and important to understanding today's variety of landforms. For instance, researchers in the Department of Earth Sciences at the Vrije Universiteit Amsterdam are studying the mechanisms leading to the formation and modification of new continental crust. This research is leading to improved estimations of the timescale of rift development and its variations, and to understanding of the relationships between magmatic processes and crustal growth. The Computational Geo-Ecology group of the University of Amsterdam is interested in how tectonic structure, due to tectonic collisions and the resulting rock and mountain formation, influences the configuration of landforms and their diversity, as well as the distribution of quaternary materials and soils.

The Royal Society of London held the world's first symposium on plate tectonics only as recently as 1964. If Wegener had reached the age of 84, he would have certainly been invited as a guest of honour, as although Wegener's mechanism and rates of continental drift have since been corrected, his creativity and originality first painted a picture of continents on the move. Wegener was the first to think of the continents we walk on today as stone drafts, drifting through the oceans as fast as our nails grow. Ω

"The continents must have shifted,' Wegener wrote"



← **Figure**
The movement of magma beneath the Earth's crust continuously pushing the continents apart. Still from the BBC documentary film 'Earth: The Power of the Planet', available online via https://youtu.be/ryrXAGY1dmE. Further background information can be accessed via http://www.thegeographeronline.net/.

Link
The second edition of Wegener's book, in German, is freely available at http://www.gutenberg.org/ebooks/45460

→ **Reference**
A. Wegener, The Origin of Continents and Oceans, translated from German by John Biram (Dover, New York, ed. 17, 1966).

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Testing Einstein's general relativity with neutron stars

→ The theory of general relativity as proposed by Albert Einstein offers the simplest description of particle motion in gravitational fields that is in correspondence with astronomical observations. Applying it to accurately describe the orbits of GPS satellites around Earth has helped me pinpoint my grandmother's house on more occasions than I would like to admit. But Earth's gravitational field only qualifies as weak when viewed on an astronomical scale. To prove the universality of general relativity, we need to test its predictions in more extreme environments.

© MARIEKE VAN DOESBURGH performed this research while a MSc student at the Anton Pannekoek Institute for Astronomy, UvA, where she is now a PhD student.

Neutron stars as a laboratory

Enormously dense neutron stars can contain up to twice the mass of the Sun packed into a sphere of only 10 km radius, and they offer the ideal circumstances for such a test of general relativity. Neutron stars can rotate as fast as once every millisecond and, while they do not themselves shine like our sun, they have other mechanisms by which we can see them in the night sky. Often they are accompanied by a nearby star, from which the neutron star pulls away gas, as the surface gravity of the stellar companion is no match for the extreme gravitational attraction of the compact neutron star. In this process, known as accretion, a lot of energy is released in the form of X-rays. While we cannot spatially resolve the neutron stars themselves, as they are too small and too far away, we can count the number of X-ray photons we receive over time. Typically, this X-ray signal varies as a function of time, and using mathematical tools we can uncover hidden patterns in the X-ray intensity.

One of the patterns we discover is a strictly periodic, lighthouse-like signal. Localized hotspots on the surface of the neutron star that spin in and out of view offer an explanation for this periodicity. When we see such a signal, the neutron star's rotation rate can thus be obtained. In addition to this strictly periodic contribution to the signal, patterns are also present that are close to periodic and do not have an off-the-shelf explanation.

"General relativity has helped me pinpoint my grandmother's house on more occasions than I would like to admit."

Link to MSc thesis

https://esc.fnwi.uva.nl/thesis/centraal/files/f1782582722.pdf (Master's Programme in Astronomy and Astrophysics, thesis work supervised by Michiel van der Klis, Anton Pannekoek Institute for Astronomy, UvA)

Lense-Thirring precession

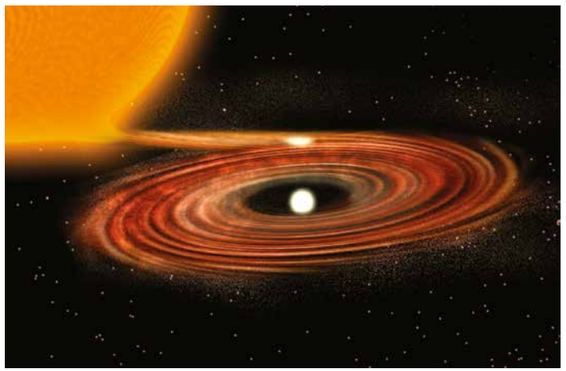
In the framework of general relativity, a rotating object drags along and deforms spacetime. YouTube's enthusiastic physics teachers have helped me visualize this by pouring their marble collection onto a sheet of spandex stretched over a hula hoop (well worth the web-surfing expedition; search for 'Gravity Visualized'). The spinning marbles will form a dent in the improvised spacetime fabric and slightly twist it. In a way, the amount of twist depends on how fast the marbles spin. General relativity predicts that under certain circumstances the gas that falls onto the neutron star will precess, or 'wobble' (like a spinning top) due to the twisting of spacetime. It is this effect, called Lense-Thirring precession, that offers a possible solution for the quasi-periodic features we see in the X-ray signals. The precise pattern of the features is predicted to correlate with the spin of the neutron star, and also with the rate at which the gas orbits the star. By comparing the observational findings with theoretical predictions we are now able to test general relativity under extreme gravitational conditions.

Testing general relativity

In previous research at our institute, this test was carried out by examining the X-ray signal from three neutron stars. A correlation remarkably close to the theoretical prediction was found. Surprisingly, no effect due to difference in the rotation rate of the three stars could be discovered. In my Master's thesis project, I re-examined these findings in an extended data-set containing 21 X-ray sources and indeed found correlations. However, these are significantly different from what the theory predicts. Although the correlations vary among sources, this variation cannot be ascribed to the different rotation rates of the neutron stars investigated.

It is only fair to note that the theory predictions take single gas particles into account that reside in a vacuum, while real gas flows are more complex entities involving, for example, hydrodynamic processes. Apart from this reason for a deviation between observation and theory, magnetic effects and precession –due to the fact that a neutron star (just like the Earth) need not be a perfect sphere– can also affect the signal we are observing.

My research fuels speculation about what the mechanisms might be that cause the different types of variability we find in the X-ray emission from accreting neutron stars. Lense-Thirring precession is still thought to contribute, but to what degree, and whether general relativity indeed survives in extreme gravitational fields, still remain to be seen. Ω



→ Figure

The strong gravitational field of a neutron star (right) pulls gas away from the surface of a nearby star (left) to form an accretion disk.

Photo credit

P. Marenfeld/NOAO/AURA/NSF

The war within our DNA

© FRANK JACOBS, Assistant Professor in the Molecular Neuroscience group, Swammerdam Institute for Life Sciences (SILS) of the UvA.

→ Throughout evolution, the human DNA has been invaded by multiple classes of ancient retroviruses. These viruses have become extinct long ago, but their DNA traces still linger in our genome, where they have given rise to what we now call retrotransposons. These virus-like genetic elements have maintained the ability to multiply and insert new copies of themselves into our DNA. New retrotransposon insertions can disrupt genes and cause disease, which forces us —the host genome— to come up with mechanisms to prevent these molecular jumping events.

Genetic cat-and-mouse games

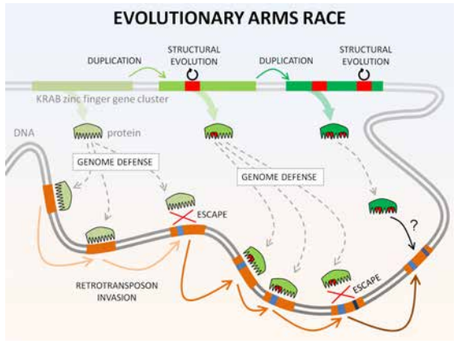
Retrotransposons are responsible for the vast majority of non-coding DNA in our genome, often referred to as junk DNA. Throughout primate evolution, retrotransposons have frequently changed their basic composition, a phenomenon reminiscent of the evolution of viruses to evade detection by the host. Because the majority of retrotransposons seem to be efficiently repressed, we know that a defence mechanism must exist in the host genome that restricts the invasion of each newly modified retrotransposon type. The mechanism that 'chases' the retrotransposons has remained elusive for a long time. Pioneering work in the labs of Stephen Goff and James Thomas suggested that so-called KRAB zinc finger (ZNF) genes — encoding a large family of transcriptional repressor proteins — are involved in the genome's defence against retrotransposon invasions. The human genome harbours more than 400 KRAB ZNF genes. Almost half of these — 170, to be exact — exist only in primates. Therefore, we and others hypothesised that the unusual expansion of KRAB ZNF genes in primates is the result of evolutionary pressure on these species to deal with new, primate-specific retrotransposon invasions.

In our study, we took on the challenge to identify the genes that have evolved to repress two classes of primate-specific retrotransposons that have been active throughout the so-called great ape evolution. After multiple years of searching, using different genetic approaches, we identified two primate-specific KRAB ZNF genes, ZNF91 and ZNF93, which evolved to repress these retrotransposons. In both cases the ancestral versions of these KRAB ZNF genes had already emerged in our genome just before the invasion of the retrotransposon started. By looking at the composition of these genes in other primates we found that soon after the invasion of the new retrotransposons began, the dedicated KRAB ZNF gene rapidly evolved to specifically recognize and repress these new retrotransposons. This success did not mean, however, that the battle was won. Although repression initially severely restricted the retrotransposon in its actions, it was not completely defeated and we found evidence that one of the retrotransposons eventually managed to escape repression of ZNF93 by simply shedding the ZNF93 binding site a few million years further down the evolutionary road. This event gave rise to a new retrotransposon element that is still actively copying and pasting itself in our genome today.

The specific example described above is just a snapshot of a never-ending race (Figure 1). KRAB ZNF genes have been rapidly expanding and evolving in primate genomes, precisely because the retrotransposons are continuously evolving to escape their repression. When retrotransposons manage to do so, the host cannot allow the KRAB ZNF gene in charge of repressing the old element to co-evolve with this change, as it would release the repression of the old elements. Furthermore, the different KRAB ZNF genes also obtain other functions and become essential for normal cellular functioning. So, instead, a newly duplicated KRAB ZNF gene needs to step up to the challenge and rapidly evolve to become the repressor of the newly emerged retrotransposon subtype, driving the genome and gene regulatory networks to a progressively more complex state.

Brainy retrotransposons escape repression

For unknown reasons, retrotransposons are less efficiently silenced in brain cells than in other cell types. This suggests that recent retrotransposon insertions could affect gene expression in the human brain, raising all sorts of new, intriguing questions. How well is the gene-regulatory effect of retrotransposons kept under control during development and aging of the human brain? Could dysregulation of mobile genetic elements be a contributing factor to complex human neurological disorders? These are the big questions that are central to the research done in our lab at the University of Amsterdam right now. Using embryonic stem cell-derived cortical tissues from human and monkey origin, our lab currently investigates how retrotransposon invasions have reshaped the gene regulatory networks involved in human brain development. Our research explores the possibility that evolutionary novelties such as retrotransposon insertions may directly relate to humans' increased susceptibility to neurodevelopmental disorders such as autism and schizophrenia and disorders associated with the aging brain such as Parkinson's and Alzheimer's. If successful, these studies will have a big impact on our thinking about complex human brain disorders. Ω



→ References

F.M.J. Jacobs, D. Greenberg, N. Nguyen, M. Haeussler, A.D. Ewing, S. Katzman, B. Paten, S.R. Salama, D. Haussler, An evolutionary arms race between KRAB zinc-finger genes ZNF91/93 and SVA/L1 retrotransposons. *Nature* 516, 242-245 (2014).

Putting Higgs on the scales

STEFAN GADATSCH graduated *cum laude* as a PhD student from Nikhef/UvA in June 2015.

→ We regularly hear of *competing* experimental data from the two big experiments at the Large Hadron Collider (LHC) in Geneva - called ATLAS and CMS. However, when data from these experiments are *combined*, the results can be especially powerful.

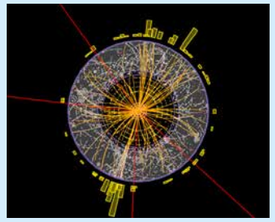
No one will have missed the LHC's recent discovery of the Higgs particle, which completes a vital part of the Standard Model of subatomic physics, providing an explanation as to why we (and all other matter) weigh anything at all. But how much does the Higgs particle itself weigh? The ATLAS and CMS teams joined forces to measure the Higgs mass with unprecedented accuracy, an endeavour involving researchers at Nikhef, the National Institute for Subatomic Physics in Amsterdam, and the UvA via their work on ATLAS. As a PhD researcher, I was heavily involved in the analysis that appeared in the premier physics journal *Physical Review Letters* in May 2015.

When Higgs particles decay, they send out other elementary particles we can detect. 'My' ATLAS team and our CMS colleagues merged the analyses of two such decays: one into two particles known as Z bosons ('ZZ' decay), and one into two photons ('gamma gamma' decay). Merging these decays enabled a highly accurate estimate of the Higgs mass. Particle physicists like to express mass in energy units (referring to the famous equation by Einstein linking energy and mass), and the Higgs particle weighed in at 125.09 billion electron volts, which is more than two atoms of iron taken together. This value was measured with an uncertainty of only 0.2%.

Run 2 of the LHC, which just started, is expected to enable a further squeeze of the experimental uncertainties, but the present number already shows that the Higgs mass is very special. With this value, either our universe is not stable and close to a phase transition, or the Standard Model is wrong. Thus rather than being finished, the Higgs story is only just beginning.... Ω

→ Reference

G. Aad et al., (ATLAS Collaboration, CMS Collaboration), Combined Measurement of the Higgs Boson Mass in pp Collisions at √s=7 and 8 TeV with the ATLAS and CMS Experiments. *Phys. Rev. Lett.* 114, 191803 (2015).



↑ Figure
Graphical representation of a Higgs decay event, in this case into 4 muons.

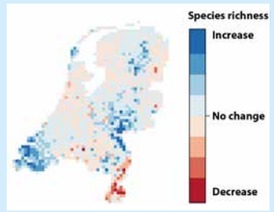
Historical landscapes influence biodiversity in today's pollinators

JESÚS AGUIRRE GUTIÉRREZ is a PhD student at the Naturalis Biodiversity Center and the Institute of Biodiversity and Ecosystem Dynamics [IBED] of the UvA.

→ Pollinators like bumblebees, butterflies and hoverflies support the production of 75% of crops as well as the reproduction of wild plants and trees. Countries around the world are experiencing declines in pollinator species at alarming rates, largely because of the transformation of landscapes. During the last century, landscapes everywhere have changed, sometimes in unimaginable ways. In highly industrialized countries like the Netherlands, forests have been turned into farmlands, flood lands and lakes into flatlands (*polders*), and many natural habitats into urban or agricultural areas. These landscape transformations may have an important temporal effect by affecting species richness in the present. How the current biodiversity resulting from these changes affects pollinators is yet unknown.

To investigate the influence of landscapes on the distribution of pollinator species richness, we coupled historical data (1930-2009) on changes in species richness of three pollinator groups (bumblebees, butterflies and hoverflies) with data (1900-2008) on changes in land use representing landscape composition, fragmentation and the potential for animal movements between different landscapes, that is, the spill-over potential. We discovered (1) how different pollinator groups have responded differently to landscape changes, (2) how current species responses to landscape changes are influenced by historical landscapes, and (3) how, for most pollinator groups, historical landscape characteristics influenced recent changes in species. Bumblebee species richness benefited from increases in borders between managed and natural land; wild bees benefited from increases in total landscape heterogeneity. Bumblebee species richness was most susceptible to ecosystem fragmentation events. Landscapes that had experienced changes that attracted diverse animal species were more likely to exhibit declines in butterfly species richness. Hoverfly species richness, on the other hand, was resistant to landscape changes.

Our results illustrate how the role of humanity as modifier of the biosphere affects the temporal distribution of biodiversity. Moreover, future responses of pollinators to landscape changes will most likely depend on the landscape conditions we create today. Ω



↑ Figure
Changes in bumblebee species richness in the Netherlands during the last century. Bumblebee species richness benefited from increases in borders between managed and natural land.

→ Reference

J. Aguirre-Gutiérrez, J.C. Biesmeijer, E.E. van Loon, M. Reemer, M.F. Wallis de Vries, L.G. Carvalheiro, Susceptibility of pollinators to ongoing landscape changes depends on landscape history. *Diversity Distrib*. 21, 1129–1140 (2015).

Green computer networks

© PAOLA GROSSO Assistant professor in the System and Network Engineering [SNE] group at the Informatics Institute, UvA.

→ **We all use the internet daily, without really being concerned about the paths taken by our data to reach their destination. We all communicate continuously without explicitly checking the behaviour of the devices that move our bits and bytes. All of this is bound to change, as we no longer want to waste energy this way. Thanks to new technologies and protocols, the networks of the future will operate differently than today. For the people and companies interested in exploiting these new possibilities and aiming for a greener ICT, the internet will no longer be just a black box that cannot be adjusted.**

Right now, networks are becoming directly programmable from applications, so that individual users can decide on the paths followed by the data and on the type of services provided by the various internet nodes. This new mode of operation goes under the name of Software-Defined Network (SDN).

Computer scientists recognize the possibilities offered by SDNs: they want to identify and implement novel algorithms, leading to faster, more secure, and more responsive networks. Among many new uses, SDNs offer the possibility to create 'green' networks, i.e., networks possessing a smaller energy footprint, while maintaining the same level of performance. Green networks are in fact one of the elements required to create a sustainable computing ecosystem, also known as Green ICT. Networks, computing clouds, physical devices and software programmes can all be tuned to be more energy efficient, both individually and in combination with one another.

Research by the SNE group at the UvA focuses on green networking and green ICT. The group tries to identify the algorithms and techniques that can improve the energy efficiency of the internet. A particular focus is on those algorithms that can easily shape the network traffic in order to improve energy efficiency without degrading other quality requirements.

Green routing
Research on this aspect has been carried out by Hao Zhu, PhD researcher in the SNE group, and described in the article "Joint flow routing-scheduling for energy efficient software defined data center networks". Zhu developed a new solution to implement 'green routing' by comparing different algorithms in terms of their effect on the total power consumption of the underlying network. He integrated these green routing capabilities in an existing network-management platform - OpenNaaS (Open platform for Networks as a Service) - to make a centralized routing decision for scheduling traffic and to configure the forwarding rules. To achieve energy-awareness in the system, he augmented OpenNaaS with monitoring and description capabilities based on the Energy Description Language (EDL). EDL is an ontology developed in the SNE group that allows deeper reasoning based on the energy data available, so that users and applications can take more complex decisions in programming the network.

The Figure shows the chosen energy-efficient network route (green line). This route is selected using data gathered from power meters in the network; to program the correct behavior in the network devices. OpenNaaS relies on SDN controllers, which communicate with the network switches (SW in the Figure) to generate the desired traffic flow directions.

Green software
What is coming next? As networks are only the fabric supporting the computing and data movements, energy efficiency also requires green data centres and green software. Fahimeh Alizadeh, a joint PhD student of the UvA's SNE group and the Software Services group at the Vrije Universiteit Amsterdam, is now looking at the integration of all these components to allow distributed applications running in clouds to programme SDNs. Her initial work has already resulted in a publication entitled "Energy efficient networking solutions in cloud-based environments: a systematic literature review" in the prestigious journal *ACM Computing Surveys*.

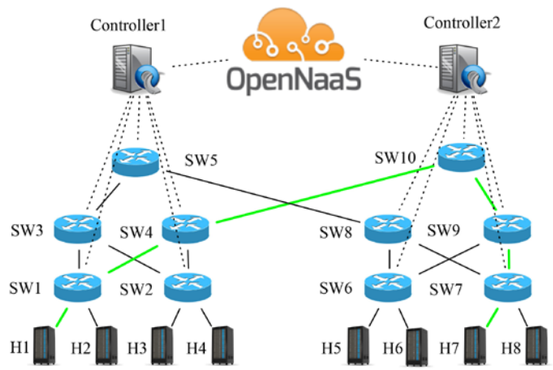
Green Networks
The SNE group has been involved in several national and international collaborations on this topic. Among them, two projects were rooted in Amsterdam: the 'Green Software' and 'Greening the Cloud' projects, both of which also involved the participation of the Vrije Universiteit Amsterdam (VU) and the Amsterdam University of Applied Sciences (HvA.). These joint efforts highlight the leading role Amsterdam and its research institutions have in the subject of sustainable computing. Ω

"Computer networks; smaller energy footprint, same performance"

→ References

F. Alizadeh Moghaddam, P. Lago, P. Grosso, Energy-efficient solutions in cloud-based environments: a systematic literature review, *ACM Computing Surveys* 47, 64 (2015), available online at http://dl.acm.org/citation.cfm?id=2764464

H. Zhu, X. Liao, C. de Laat, P. Grosso, Joint flow routing-scheduling for energy efficient software defined data center networks, to appear in *Elsevier Journal of Network and Computer Applications*.



Plant hairs up close

In the greenhouse of the Amsterdam Science Park tomato plants can be found in abundance. Under a microscope it becomes clear that their green parts are covered with hair-like structures, called trichomes. The 'heads' of some of these trichomes function as small chemical factories, producing toxic and volatile substances. If we touch the plant, these cells rupture and volatile compounds are released, causing the characteristic tomato odour. In nature, herbivores foraging on the plant cause the release of tomato volatiles, which serve as the plant's 'cry for help' and attract the enemies of the herbivore. The Plant Physiology group of the UvA investigates the potential of these natural defence compounds in wild and cultivated tomato plants.

Image
JAN VAN ARKEL
Photographer at the Institute for Biodiversity and Ecosystem Dynamics [IBED], UvA.

Research
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Repairing the retina: a gene-therapeutic approach

PETER M. QUINN
PhD Student in Retinal Degenerative Diseases at the Netherlands Institute for Neuroscience, Amsterdam.

→ **Blindness is a debilitating disease that affects millions of people worldwide. Scientific advancement is, however, laying the foundations to combat such diseases using retinal prostheses as well as cell- and gene-therapeutic approaches. The first step on the road to developing any therapy is to understand the underlying disease mechanisms and how they might be manipulated. For over a decade our group has tried to answer these fundamental questions using mice that mimic hereditary blindness, providing a platform from which we have developed therapeutic tools for their treatment. Now, using gene therapy, we have successfully replaced faulty genes in our mouse models. By doing so we were able to change the disease's natural course, leading to improved retinal functionality.**

The retina and hereditary blindness

The retina is a multilayered tissue at the back of the eye, which receives light cues that then travel through the optic nerve to be interpreted by the brain. The retina contains seven cell types, including the light-sensitive photoreceptors and the neuronal support Müller glial cells (see the Figure). The photoreceptors are of two types: rods, for vision in dim light, and cones, for higher light levels and colour vision. There are over 160 genes associated with hereditary eye diseases. We focus on two genes, CRB1 and CRB2, which are involved in the control of adhesion between photoreceptors and Müller glial cells. Mutations in the human CRB1 gene lead to disruption of this adhesion resulting in both congenital and early-onset diseases such as Leber Congenital Amaurosis and Retinitis Pigmentosa - eye disorders that cause visual impairment.

CRB fundamentals

The CRB1 and CRB2 proteins have similar structures and are localised at junctions between the photoreceptors and the Müller glial cells, residing at the outer limiting membrane (which is the multicoloured layer at the top of the Figure). Loss of CRB proteins leads to a dysregulation of the cell cycle during retinal development and subsequently to disruption of adhesion between Müller glial cells and photoreceptors, This causes retinal disorganisation, resulting in disease.

Which genes to target in which cells?

With a better understanding of the molecular basis of CRB-related retinal diseases we set out to create possible gene therapy tools. We used mice with different levels of retinal integrity to verify whether we could bring back proper cell adhesion, leading to improved functionality. In gene therapy a faulty gene is replaced with a 'healthy' copy. In our case, we packaged a correct version of either CRB1 or CRB2 into viral particles that were then injected into the diseased retina. Our system was cell-specific, meaning that we were able to target the correct gene to certain cell types in the retina, namely the Müller glial cells and/or photoreceptors. Success was measured in terms of improved retinal function and the preservation of its architecture as compared to control models. When targeting both cell types with the CRB2 packaged viral particles, signs of a recovery were clear. However, when targeting either Müller glial cells or photoreceptors alone, no improvement was found, suggesting that the CRB2 needs to be present in both cell types to mediate their adhesion. Furthermore, when targeting the two cell types either individually or together with CRB1 instead of CRB2, we found *reduced* retinal function. In fact, we observed an immune reaction, which was initially surprising, as the eye is generally considered to be immune privileged, meaning it is more likely to tolerate foreign antigens. We believe that the injected human CRB1 was rejected, most probably due to the influence of the diseased retina.

Hypothesis vs. reality: moving into the future

While our research has made a case for targeting multiple cell types at the same time and highlighted possible immune reactions, long-term efficacy issues in clinical gene therapy for other retinal disease genes have been identified as well. Recent clinical retinal gene therapy trials have shown that this approach may only provide a temporary benefit, lasting three years. In addition, treating patients whose eyesight has already started to degenerate presents a further challenge, mainly to slow down the photoreceptor cell's death. However, providing any benefit and extending vision for even a few years is still a step in the right direction.

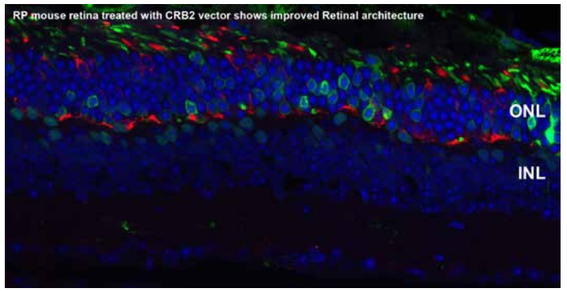
After our initial experiments, we now need to test the long-term efficacy of our therapy and its potential use in congenital blindness. We hope to be moving towards preclinical testing at the end of 2016, thereby taking the next step on the long road towards an approved treatment. Ω

→ **References**

1] L.P. Pellissier, P.M. Quinn, C.H. Alves, R.M. Vos, J. Klooster, J.G. Flannery, J.A. Heimel, J. Wijnholds, Gene therapy into photoreceptors and Müller glial cells restores retinal structure and function in CRB1 retinitis pigmentosa mouse models. *Hum. Mol. Genet.* 24, 3104-18 (2015).

2] L.P. Pellissier, C.H. Alves, P.M. Quinn, R.M. Vos, N. Tanimoto, D.M. Lundvig, J.J. Dudok, B. Hooibrink, F. Richard, S.C. Beck, G. Huber, V. Sothilingam, M. Garcia Garrido, A. Le Bivic, M.W. Seeliger, J. Wijnholds, Targeted ablation of CRB1 and CRB2 in retinal progenitor cells mimics Leber congenital amaurosis. *PLoS Genet.* 9, e1003976 (2013).

↓**Figure**
Mouse retina that originally lacked CRB2 genes were injected with a fluorescently labelled human CRB2 vector (in green). This gene therapeutic approach preserves the healthy retinal architecture, resulting in robust and well-organized layers. The cell nuclei are stained blue, the cones red.



"I had to pinch myself a few times."

© FRED JANSEN
Dr Fred Jansen studied Astrophysics at the UvA. He obtained his PhD at Leiden University on a study of X-ray radiation originating from the remainders of supernovae. He worked at the Netherlands Institute for Space Research [SRON] and the European Space Agency [ESA] on the XMM-Newton mission. After that Dr Jansen was project scientist at the ESA's Mars Express and Venus Express, and mission manager of both XMM-Newton and Rosetta. Rosetta was launched in 2004, rendezvousing with the comet 67P ten years later and releasing the Philae lander to make the first-ever soft landing on a comet.

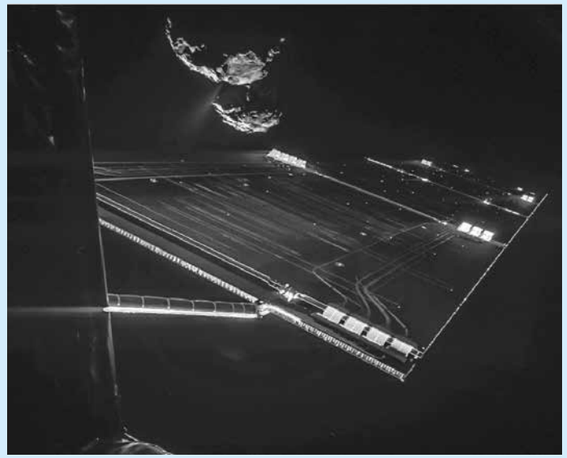
→ The past two years have been the most tiring, difficult and rewarding ones in my scientific career. In May 2013 I was asked to join the Rosetta mission as mission manager – the person carrying overall responsibility for the project. The objective: to deliver this scientific mission of the European Space Agency (ESA) to the comet 67P/Churyumov-Gerasimenko, escort it for 16+ months and land its Philae probe on the comet. Fifteen months and a lot of difficult decisions, compromises, travel and incredibly hard work later, I found myself in our control centre in Darmstadt, Germany along with 200+ media teams from all over the world, streaming live from there to events all over Europe, including one at the Parc des Sciences in Paris – with the French president Hollande. To cut a long story short, we successfully landed on the comet that day and I had to pinch myself a few times to realize this was all true. When I called my wife later that day the only thing we could both do for some 20 minutes was cry.

After this event and the associated media hype many, many invitations followed to present and share this amazing story. For me the absolute highlight of this was an invited presentation at the TED annual conference in Vancouver in March. The presentation was put online and has been viewed some 900,000 times.

This story of successive opportunities coming my way begins in August 1976 when I entered the 'Roeterseiland' building of the UvA to start studying astrophysics. For my graduation research project Professor Ed van den Heuvel put me in touch with a group in Leiden: they needed somebody practical/computer-oriented for a collaborative project with MIT. This worked well and I got asked to do my PhD in Leiden. Afterwards I spent some years in the lab with no clear options for the future. In 1995 I got asked to join ESA and this eventually led me to managing XMM-Newton, Mars Express, Venus Express, Rosetta and now Gaia; all amazing science missions.

This past summer, some 39 years later, my son, together with hundreds of others, went to the 'Roeterseiland' for the introduction week as the start of his own university study. If, as a society, we want to get the best out of these young people, opportunities will have to exist for them to experience 'thinking outside of the box', to learn, grow and realise their own potential. If we don't manage to do this, part of the investment in them will be lost. Ω

→**Figure**
Selfie of the Rosetta spacecraft, taken at a distance of 16 km from the surface of the comet (visible in the background).



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A 'spin-off' is a company that is formed on the basis of a specific scientific invention. Spin-off companies make it possible for fundamental knowledge that is developed by institutes to make its way to society, resulting in topquality jobs.

Science spin-offs Amsterdam 2015

CHEMISTRY

UvA

InCAtt
Plantics

HEALTH

NKI

Agendia N.V.
Amsterdam Biotherapeutics unit AmBtU
Ceronco Biosciences
Modra Therapeutics
UbiQ Bio BV
Qamelon Therapeutics BV

AMC

Arthrogen
Caelus Pharmaceuticals
Forensic Technical Solutions
Hep-Art Medical Devices
Microvision Medical
mirNext / ACS Biomarker
Regenesance
Sigmascreening
AIMM Therapeutics
Inreda
Mediphenix
uniQure
Photonics
Haermonics

ACTA

AM Pharma BV

VU

Iota Pharmaceuticals Ltd.
Mucosa BV
Griffin Discoveries BV

VUmc

2QR Research BV
AngioTarget BV
A-Skin Nederland BV
Cyclotron Vrije Universiteit BV
DC4U BV
DCPrime BV
Evalua Nederland BV
GeriMedica BV
Microbiome Ltd.
Mucosa BV
Preselect Diagnostics BV
Somantix BV
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UvA

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OPNT BV

AMOLF, TUDELFT

Delmic

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GreenA

INFORMATICS

UvA

Sightcorp
904Labs
Scyfer
3Duniversum
Perceptech
Electric Ant
Quva lab (met Qualcomm)
Whitebox

CWI

MonetDB Solutions
Spinque
MonetDB B.V.
Safiro Software Solutions
Personal Space Technologies
Adaptive Planet
Software Improvement Group (SIG)
Unipay Technologies
SIDN
CAN Diensten

VU

Scientific Computing & Modelling NV

Disclaimer: although the utmost care has been taken, omissions or inaccuracies can be possible, due to the highly dynamic nature of the start-up landscape.

Photo credit: KEES VAN WENSEN

Microbes strike back: How bacteria develop antibiotic resistance

→ Reports on antibiotic-resistant pathogenic microbes are rising alarmingly in the last decade → **Figure 1**. The costs of treating patients infected with antibiotic-resistant microbes are tremendous and still steadily increasing every year. Treatment of patients who are infected with a resistant pathogen is lengthy and much more expensive compared to non-resistant pathogens. Since the discovery of penicillin, nearly a century ago, the use of antibiotics has grown very rapidly, not only for treatment of bacterial infections in humans, but also on a large scale in animals. In recent years, veterinary use of antibiotics in the Netherlands has been reduced to half of that in 2007, still totalling 200 tons sold for therapeutic use. In addition, use of antibiotics as growth promoters has been banned in the European Union since 2006. Nonetheless, with the dramatic increase of exposure to antibiotics, microbes have evolved strategies to become and remain drug resistant. This article highlights recent findings of how bacteria can evolve their resistance on the molecular level.

NADINE HÄNDEL
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MERIJN SCHUURMANS
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"All roads lead to bacterial resistance to antibiotics"

Drug resistance

Drug resistance in microbes is not a recent phenomenon. Analysis of ancient DNA isolated from 30,000-year-old Beringian permafrost sediments demonstrated the existence of a highly diverse collection of genes encoding resistance to many different antibiotic classes. Still, the misuse of antibiotics in the past twenty years has created a selective advantage for the acquisition of antibiotic resistance genes, which have dispersed to a variety of different bacterial species. The repertoire of antibiotics available for healthcare is limited, and since innovative treatment strategies or the development of new antimicrobial components are lagging behind, international organisations, such as the World Health Organization (WHO), raised the alarm about the increasing number of drug-resistant microbes. The European Commission estimated in 2011 that within the EU antibiotic resistance in pathogenic microbes caused 25,000 human deaths annually and extra healthcare costs and productivity losses of at least € 1.5 billion per year.

Bacteria can become resistant through three main mechanisms → **Figure 2**: (1) Physiological adaptation - for example, bacteria can increase the expression of transport proteins that actively extrude antibiotics out of the cell or increase expression of an antibiotic degrading enzyme; (2) Genetic adaptation - due to mutations in their DNA, cells can become less sensitive to an antibiotic that originally inhibited its cellular processes (drug target); (3) Through transfer of resistance genes from other bacteria. To curb the continuous rise of drug-resistant bacteria worldwide, new strategies are urgently needed that counteract the development and spread of resistance. We studied the relationship between antibiotics use and the development of resistance, using laboratory cultures of the bacteria *Escherichia coli*. This is a very well-studied gram-negative bacteria commonly found in the human gut, and an established model organism for bacteria in general.

Resistant *E. coli*

In order to study the transformation from antibiotic-sensitive to antibiotic-resistant cells, *E. coli* was made resistant by stepwise increasing the antibiotic concentration whenever the cells could still grow. Adaptation to very high drug concentrations was observed for different classes of antibiotics within only 14 days. For example, the minimum inhibitory antibiotic concentration as a measure of drug sensitivity increased 12-fold for the fluoroquinolone antibiotic enrofloxacin. Enrofloxacin is an antibiotic that is more commonly known as Baytril and is often used for the treatment of ear infections in domestic animals. During a 1-month study, *E.coli* cells could adapt to a 100-fold increase in concentration of enrofloxacin.

→ **References**

1] Nathalie Händel, thesis: Quantitative relationship between antibiotic exposure and the acquisition and transmission of resistance in bacteria in the laboratory (2015). Available online via: http://dare.uva.nl/record/1/446010

2] Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands (MARAN) report 2015, see http://www.wageningenur.nl/upload_mm/2/2/2/0ab4b3f5-1cf0-42e7-a460-d67136870ae5_NethmapMaran2015.pdf

3] N. Händel, J.M. Schuurmans, Y. Feng, S. Brul, B.H. ter Kuile, Interaction between mutations and regulation of gene expression during development of *de novo* antibiotic resistance. *Antimicrob. Agents Chemother*. 58, 4371-4379 (2014).

4] N. Händel, J.M. Schuurmans, S. Brul, B.H. ter Kuile, Compensation of the metabolic costs of antibiotic resistance by physiological adaptation in *Escherichia coli*. *Antimicrob. Agents Chemother*. 57, 3752-3762 (2013).

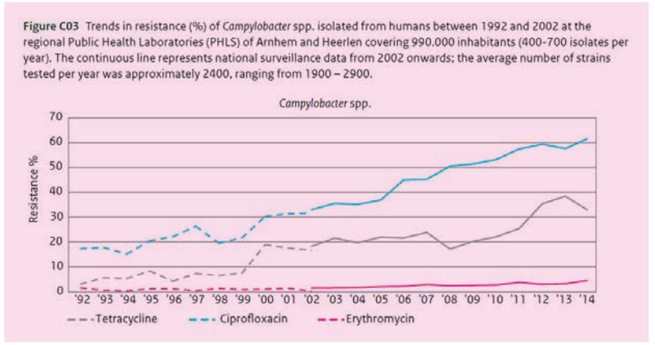
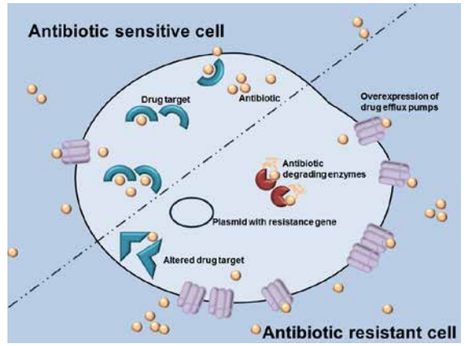


Figure C03 Trends in resistance (%) of *Campylobacter* spp. isolated from humans between 1992 and 2002 at the regional Public Health Laboratories (PHLS) of Arnhem and Heerlen covering 990.000 inhabitants (400-700 isolates per year). The continuous line represents national surveillance data from 2002 onwards; the average number of strains tested per year was approximately 2400, ranging from 1900 – 2900.



Thus, we could double the antibiotic concentration in the culture medium almost every day without killing the bacterial population.

Enrofloxacin normally performs its antibiotic task by blocking two key enzymes involved in bacterial DNA replication. The resistant *E. coli* population contained genetic mutations specifically in these two key enzymes. In the resistant population, enrofloxacin can no longer bind to these two key enzymes and as such it can no longer inhibit their function, allowing normal replication of DNA and cell growth. Resistance, however, comes at a cost, as the resistant strains have a slightly lower growth rate in the absence of the antibiotic.

At low, sub-lethal concentrations, antibiotics can trigger specific mechanisms that allow for intentional error-prone DNA replication. This response, aptly named 'SOS response', transiently increases the mutation rate of the bacterial DNA. Under non-stressed conditions, the mutation rate is kept low, as the cells are already well adapted to their current conditions. Under stressful conditions, however, an increase in mutation rate can enhance the probability of generating a successful adaptive mutation, re-establishing the growth and propagation of the bacterial population. We tested whether a functional SOS response is required for *de novo* acquisition of resistance by using bacterial strains in which this SOS response was genetically inactivated. We found that the importance of the SOS response is strongly dependent on the class of antibiotics applied to the bacterial culture. If the development of resistance requires the change of a cellular protein by means of DNA point mutations, a lack of the SOS response prevents the acquisition of drug resistance. For acquisition of resistance that is not dependent on gene mutations, the SOS response can slow down the process but it is not essential.

↖ **Figure 1**
Trends in resistance (%) of *Campylobacter spp*. isolated from humans between 1992 and 2002 at the regional Public Health Laboratories (PHLS) of Arnhem and Heerlen covering 990.000 inhabitants (400-700 isolates per year). The continuous line represents national surveillance data from 2002 onwards; the average number of strains tested per year was approximately 2400. Source: MARAN report 2015.

↗ **Figure 2**
Main mechanisms of antibiotic resistance in bacteria. Genetic changes in proteins that are targeted by the antibiotic (altered drug target), acquisition of mini-chromosomes carrying resistance genes (plasmid with resistance gene), development of enzymes that break down the antibiotic (antibiotic degrading enzymes), removal of the antibiotic from the cells (overexpression of drug efflux pumps).

Is the way in which antibiotic resistance develops fixed, or are there more ways to achieve this goal? Thanks to new DNA-sequence technology we were able to address this question. By following the mutation pattern over the course of resistance development we discovered that different combinations of mutations occur in biological replicates. This indicates that there is no fixed pathway leading to high-level enrofloxacin resistance. Independent of the kinds of mutations, the outcome was always the same: high-level resistance.

Gene expression

Next to the analysis of genetic mutations that occur during the acquisition of antibiotic resistance in *E.coli*, we also investigated whether expression levels of genes changed. For a cell to make proteins (in other words: to express a gene), a gene first has to be copied into RNA in a process known as 'transcription'. When or in what quantity a protein has to be produced is determined largely by the number of mRNA molecules that are transcribed from a particular gene. Using a whole-genome mRNA expression analysis, we identified permanent changes in expression levels of certain genes in resistant cells. These permanent changes in transcription levels of certain genes were neither independent of continued antibiotic exposure nor fixed by mutations. Thus, regulation at the transcriptional level (quantitative changes: different numbers of mRNAs) appears to be just as important as the acquisition of resistance conferred by mutations (qualitative changes: mutated proteins). Some of the genes producing increasing amounts of certain proteins ('upregulation') could be directly linked to antibiotic resistance, for instance the *ampC* gene, encoding for β-lactamase, which is an enzyme that can break down the penicillin-class of antibiotics such as amoxicillin. We found that this gene is approximately 100-fold overexpressed in *E. coli* cells that have become resistant to amoxicillin.

Finally, we discovered that genes coding for important global regulators that have not been described before in the context of antibiotic resistance, played an important role in the *de novo* acquisition of drug resistance. Some of these upregulated genes remained at a high level of expression even when antibiotics were removed from the culture medium.

Roads to Rome

By combining information from the genetic and transcriptional level during the acquisition of enrofloxacin resistance in *E.coli*, we were able to show that *de novo* resistance to antibiotics is brought about by a complex interaction of cellular processes, involving both changes in transcription levels and DNA point mutations. Bacterial cells apparently have a remarkable capacity to develop resistance to antibiotics in various ways that is reminiscent of the old saying 'All roads lead to Rome', or, in this case, 'All roads lead to bacterial resistance to antibiotics'.

Overall, our data could be deployed to optimise current treatment strategies based on the combination and alternation of different classes of antibiotics. Indeed, recent studies indicate that the use of drug cycling or alternating antibiotic treatments slow down the evolution of resistance. Clearly, there still is much potential in optimising current treatment protocols to slow down *de novo* acquired resistance in microbes and to gain control over the development and spread of antibiotic resistance. Ω

Spotlight on friction at the atomic scale

TOMISLAV SUHINA is a PhD student at the Molecular Photonics [HIMS] and Soft Matter [WZI] groups of the UvA.

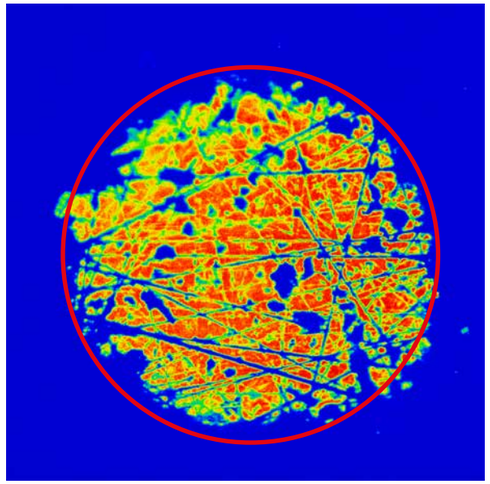
→ Estimates say that friction is responsible for around 30% of the worldwide energy consumption, yet it is still poorly understood scientifically and difficult to predict. Understanding friction on the atomic scale is key, as even the largest of objects ultimately touch one another at the scale of atoms. However, direct visualization of such small contacts was not possible in the past. In collaboration with the UvA's Institute of Physics, we have developed a new technique to visualise these contacts.

Our approach involves the preparation of molecules that can be chemically attached to the surface. These molecules are quite special; on their own they do not fluoresce, but as soon as they are brought in contact with another surface they light up exactly where the force is exerted on the surface to which they are attached. In our experiments we demonstrated this by bringing a plastic sphere into contact with a flat glass surface on which we previously attached our molecules, and registering the effects by fluorescence microscopy of the region where contacts take place.

Back in 1881, Heinrich Hertz gave a famous theoretical formula linking the size of contact area to the applied force. We have shown that this theory works nicely on a scale of micrometres or higher (where contacts act as if they are smooth), but we were also able to distinguish fine details within the overall contact region, which originate from the roughness of the plastic bead's surface. In this way, we visualised contacts on a molecular scale for the first time, which opens the door to deeper insight into friction.

As machines are getting ever tinier, and their moving parts must as well, they increasingly suffer from friction. This makes the kind of insight that our new method can deliver important for further successful miniaturisation of moving parts. Ω

→ Reference
T. Suhina, B. Weber, C.E. Carpentier, K. Lorincz, P. Schall, D. Bonn, A.M. Brouwer, Fluorescence microscopy visualization of contacts between objects. *Angew. Chem. Int. Ed. Engl.* 54, 3688–3691 (2015).



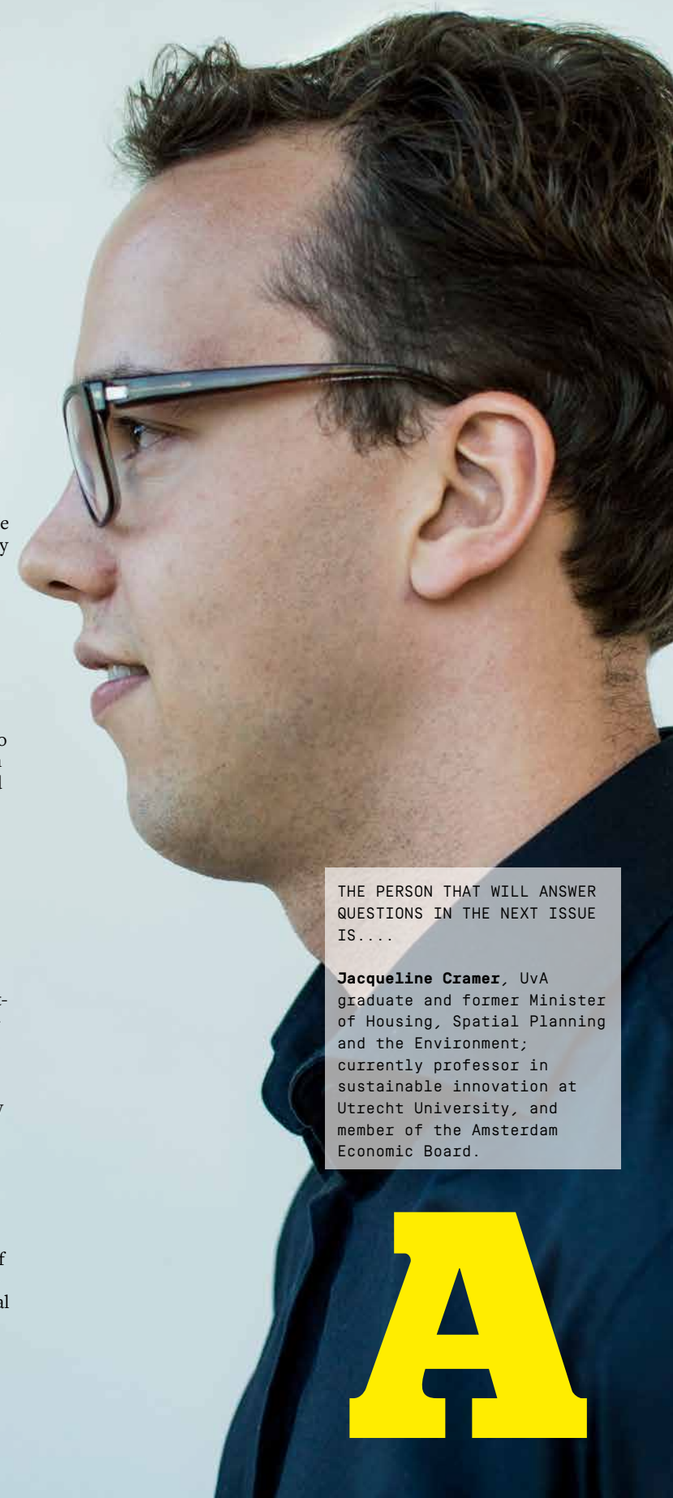
← Figure
Example of a contact-area measurement. Molecules confined between two surfaces light up, which makes contact visualization possible. The circle represents the contact area as predicted by Hertz's theory. Within the circle, fine contact structure is observable and provides additional information about the contact.

Image
Bart Weber

"Understanding friction on the atomic scale is key, as even the largest of objects ultimately touch one another at the scale of atoms."

Q

© ROGIER VLIJM
PhD student of theoretical physics and chair of the PhD Council of UvA's Faculty of Science.



1.
The first experiment I ever did was...
... for a project in high school, where we had to recreate a laser show. We deflected a laser beam with two mirrors. The perpendicular vibrations of the beam formed the ingredients of our own laser show, but first we had to find the right frequency of these vibrations.

2.
My constant source of inspiration is...
... my father. He was always there for me, stimulated me in my development, encouraged me to move into science and supported my passion for sport.

3.
One book that I recommend to all young scientists is...
... *Flatland: A Romance of Many Dimensions* by Edwin A. Abbott. It's a combination of a mathematical essay, in which the concept of dimensionality is brilliantly elaborated, and a satirical novella criticizing society in Victorian times.

4.
If I headed the Ministry of Science the first thing I would change is...
... to allocate more money to fundamental research. The impact of our scientific findings on society is an important measure, but before we get there, fundamental science is key to it all. Therefore, the general direction and goals for the future of science should be set by the academic community itself.

5.
If I had to change roles with a famous person for one day, I would choose to be...
... captain of a Volvo Ocean Race boat. This year's race was particularly exciting as the boat speeds were barely differing among the boats, so that all boats were within each other's range of sight even in the middle of the Pacific Ocean. And I enjoy competing!

6.
I am most creative when...
... I take some break after being stuck or unable to track down the bugs in my programmes. After a sailing race or water polo match I get back to my research problems with a fresh mind and often find the solution quicker.

7.
If I could choose my field of study and university once again I would choose...
... Astronomy in Hawaii. For a long time I doubted between studying Astronomy or Theoretical Physics. Luckily, the Bachelor's programme in Amsterdam combines them both, so I was able to postpone this decision, but for my Master's I eventually went for Theoretical Physics.

9.
When I am not being a scientist I am mostly ...
... a watersports fanatic! Most of my time off I spend on competing in sailing races on traditional Frisian barges (*skûtsjesilen* in Frisian) or playing water polo.

THE PERSON THAT WILL ANSWER QUESTIONS IN THE NEXT ISSUE IS....

Jacqueline Cramer, UvA graduate and former Minister of Housing, Spatial Planning and the Environment; currently professor in sustainable innovation at Utrecht University, and member of the Amsterdam Economic Board.

A

Ocean currents complicate climate models

PAOLO SCUSSOLINI works as postdoctoral researcher in the Risk research group, Institute for Environmental Studies, Vrije Universiteit Amsterdam.

FRANK PEETERS is a marine micropaleontologist and works as a senior researcher in the Earth and Climate cluster, Vrije Universiteit Amsterdam.

→ Fossils of marine microorganisms such as planktic foraminifera are among the cornerstones of palaeoclimatological studies. Up to now, it has been assumed that data on the local temperature and salinity of the ocean derived from the analysis of their calcareous shells represent ocean conditions above the location where they were sedimented. Together with an international team of researchers, we have – in our recent *Nature Communications* paper – reported that this assumption is far from correct.

We used high-resolution ocean circulation models to assess the current-induced spatial footprint of planktic foraminifera, validating the models by means of the analysis of fossil foraminifera shell data from two widely separated sediment core locations. The results clearly show that foraminifera in a particular sediment core, which is generally assumed to give us the record of the palaeoclimatic conditions at that location, may originally come from areas up to several thousands of kilometres away. This in turn means that the historic temperatures inferred from the sediment cores may be off by as much as 1.5–3.0 °C.

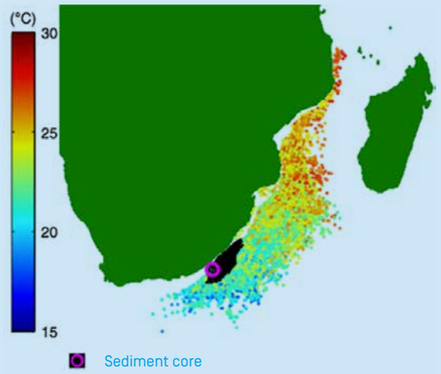
Therefore, one has to be cautious with interpreting historic oceanic temperatures from planktic foraminifera, as they originate from much larger areas than previously thought, and thus reflect an ocean state significantly different from that at the core site. This observation is both a stark warning for palaeo-oceanographers, and a powerful tool for improving climate interpretation, as since the 1950's, the earth's climate history has been reconstructed from the fossil shells of these organisms. In fact, the present study is the first rigorous investigation of the trajectories of living and settling foraminifera.

This research was a successful collaboration between European, Australian and US institutes in which two research communities – palaeo-climatologists and ocean modellers – joined forces to solve a long-standing problem. Ω

→ Reference

E. van Sebille, P. Scussolini, J.V. Durgadoo, F.J. Peters, A. Biastoch, W. Meijer, C. Turney, C.B. Paris, R. Zahn, Ocean currents generate large footprints in marine palaeoclimate proxies. *Nature Commun*. 6, 6521 (2015).

"A powerful tool for improving climate interpretation"



← Figure
Recorded temperature and oraminifera origin along a 30-day life trajectory.

The opening of QUVA lab

ARNOLD SMEULDERS
Professor of Multimedia Information Analysis at the Informatics Institute of the UvA, and co-director of QUVA.

CEES SNOEK
Associate professor at the Informatics Institute of the UvA, as well as principal engineer at Qualcomm and co-director of QUVA.

MAX WELLING
Professor of Machine Learning at the Informatics Institute of the UvA, and co-director of QUVA.

→ **By completing a jigsaw puzzle during the official opening on September 15, Senior Vice-President of Qualcomm Nagraj Kashyap and UvA Rector Dymph van den Boom marked the start of a new public-private partnership between Qualcomm and the Informatics Institute of the University of Amsterdam: the 'QUVA' lab.**

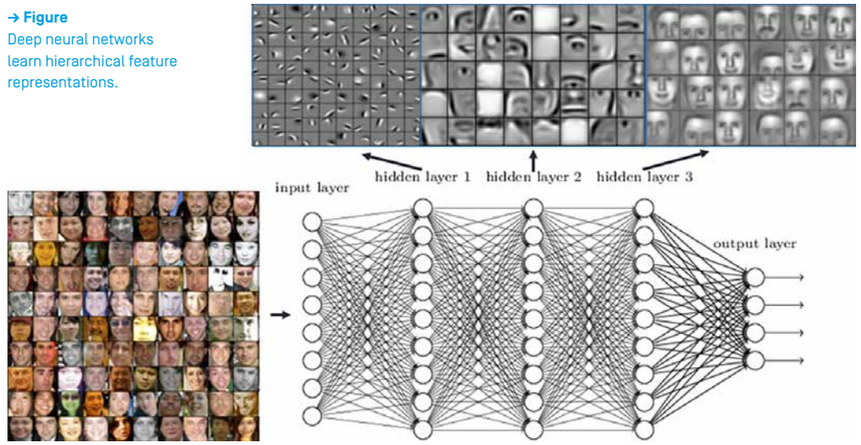
The mission of the QUVA lab is to perform world-class research on 'deep vision'. Deep-vision software should automatically interpret what happens where, when and why in images and videos, with the aid of 'deep learning'. Deep learning is a form of machine learning with neural networks, loosely inspired by how human neurons process information in the brain (see text box). Research projects in the QUVA lab will focus on learning to recognize objects in images from a single example, on personalized event detection and automatic interpretation of videos, and on privacy-preserving deep-learning tools. The aim will be to publish research results in the best academic journals, and where possible to secure novel findings in patents. The agreement between the UvA and Qualcomm will be for a period of five years and will involve the participation of 15 to 20 researchers.

One billion processors

Qualcomm Technologies, Inc. is the world-leading provider of processors and radio technology for mobile devices and especially smartphones. The company ships over one billion processors annually, which includes wireless radio processors (2G/3G/4G, WIFI, Bluetooth) as well as the CPUs, GPUs and DSPs that integrate into the Qualcomm 'Snapdragon' system-on-chip, which make your mobile devices so fabulous. Bringing computer vision together with machine learning—with an emphasis on mobile and embedded-use cases—will foster new approaches to more intelligence in smartphone cameras, robotics, automotive and Internet-of-Everything applications.

The establishment of the QUVA lab was motivated by Qualcomm's acquisition of Euvision Technologies during the Summer of 2014. Euvision was a spin-off company of the Informatics Institute of the UvA, founded and led by Arnold Smeulders. It has now become Qualcomm Research Netherlands, with its R&D team focussing on computer vision by learning. With Qualcomm Research Netherlands and the QUVA lab both located in the Informatics Institute at the Amsterdam Science Park, the development of further collaborative projects is facilitated, extending academic research in computer vision and deep learning in Amsterdam. Ω

→ Figure
Deep neural networks learn hierarchical feature representations.



Deep learning

A deep-neural computer network receives data for instance in the form of an image. It scans this image with small templates (e.g., parts of objects) that generate 'feature maps' after one layer of processing. Features represent the activities of 'neurons' that get activated if a template finds a match somewhere in the image. These fields of activities are then scanned again for suspicious correlations by new templates in the second layer of the network, resulting in new feature maps, and so forth. Where neurons in lower layers usually search for edges, neurons higher up in the hierarchy are sensitive to more abstract concepts covering a larger area of the image, such as an entire face. The final layers are trained to detect and classify the objects present in the image (for more details: read the 'VideoStory' item in the first issue of Amsterdam Science).

In recent years, new deep-learning algorithms have seen the light of day, but their backbone is still an algorithm invented in the eighties, known as 'error backpropagation'. In contrast to the feedforward processing of information necessary to detect and classify objects in images, the learning updates that tune the parameters of the network run backward through the network, computing how each synapse needs to change in order to make the network perform better. This is iterated millions of times until the updates converge. Yoshua Bengio, one of the founding fathers of the field, delivered a keynote address on deep learning during the opening of the QUVA lab on 15 September 2015.

The lifelong learner.

→ **Become a life long learner**
"Anyone who stops learning is old, whether at twenty or eighty. Anyone who keeps learning stays young." These are the words of self-taught man Henry Ford, who acknowledged the importance of continuous learning at any age. However, in daily life, formal learning for many of us is restricted to the first quarter of our lives. From primary school onwards we spend time in classrooms and lecture halls in order to enrich ourselves with knowledge. And then, all of a sudden, we are at the point of graduation, ready (or not) to take the step into working life.
Luckily for the studious amongst us, more and more initiatives arise to make education easily accessible, also for those who have long said goodbye to university. And both VU and UvA science faculties - riding the wave of the lifelong-learning trend - offer different formal and less formal ways of schooling. Below, two examples:

Summer School Programming
Over the summer, when many students enjoy their holidays, part of the UvA's Faculty of Science building is turned into a large computer lab. This past summer, more than eighty participants signed up for a week of workshops to improve their skills in programming language Ruby. One of the participants was Niels Mulder, a strategic consultant at PostNL: "I have always had an interest in programming, it is one of my hobbies. In my search for an opportunity to learn a new programming language I came across the UvA Summer School. It appealed to me that you spend a week here at the Faculty. It is great for the contact with lecturers and participants that you share an interest with."

©
ELINE VAN DILLEN
Department of Communication, Faculty of Science, UvA.

→ Info
1] www.itsacademy.nl and
2] www.uva.nl/summerschool

Its Academy
Working as a science teacher? Another initiative of the VU and UvA outside the regular educational programmes is the Its Academy, where 'Its' is short for 'informatics, technology and science'. This academy offers ongoing training for high-school teachers in the science domain. Conferences, masterclasses and networking meetings are organised to support high schools in the region and contribute to a better fit between secondary and academic education.

So, whether you wish to improve your career perspective, keep your brain fit or relive the student experience, there is always a good reason to become a lifelong learner. Ω

↑ **Figure 1** Summer School Programming. Image: Boris Ponsioen

Alumni @Work

**Where do the alumni of the Facuties of Science end up in the worldwide job market?
This item zooms in on two alumni who've moved out of academia but are still involved in and around research.**

Guus Hateboer

European Patent Attorney
at DeltaPatents

→ "Starting as a biology student at the Vrije Universiteit Amsterdam, I moved to the Bernards lab at the Netherlands Cancer Institute to become a PhD student. After a postdoc period working in a lab in Milan for two years I came back to the Netherlands. That was then when I started to have doubts about spending the rest of my working life in the lab. Coincidently, at that very same time I was writing two patent applications, which really caught my interest. I decided to completely switch careers by moving to the Intellectual Property (IP) department of Crucell in Leiden, where I was trained to become a Dutch and subsequently European Patent Attorney.

I have never regretted the move. For me it is absolutely the best of both worlds: with a scientific background in genetics, medicine and biology, I fully understand the drive that scientists have to do research. On the other hand, I now understand how to protect that knowledge, how to transfer it to a level at which it becomes 'patient-relevant', and how to deal with other (sometimes really big) parties that may either be in competition with or highly interested in the new developments. It is simply awesome to be instrumental in that process.

My job consists of a lot of different tasks: I write new patent applications, I communicate with the European patent office and foreign agents to get patents approved, and together with inventors I identify new innovations. Furthermore, I am involved in determining the 'freedom to operate' for parties that question whether their technology is part of a patent that is already filed. To stay well informed, I have to continuously keep up with the intellectual property legislation. And now and then I share this knowledge when teaching in courses about the (biotechnology) patenting process." Ω

"I fully understand the drive that scientists have to do research."

→ Insider's advice
"Scientists who have an interest in the legal aspects of their work and an affinity with its commercial relevance should certainly look into the world of intellectual property. Becoming a patent attorney does mean another few years of intense study, but for me it was all worth it."

Henriette Cramer

Research scientist
at Yahoo

→ "How people interact with systems that proactively try to anticipate their needs: that is, in short, what my research at Yahoo is about. It involves better understanding of user goals and considering the differences between machine models and people's perspectives on the world around them. Design and social expectations have a crucial impact, and it's fascinating to research that in practice.

After my PhD at the Informatics Institute of the University of Amsterdam, I moved to Stockholm to work at Mobile Life, an academic-industrial research collaboration focused on mobile systems and the Internet of Things. Mobile Life gave me the opportunity to coordinate projects on mobile and human-robot interaction. This experience gave me a much broader perspective on playful design and bodily and emotional aspects of interactions.

As a next step, I decided to immerse myself in the centre of *tech*, the San Francisco Bay Area. I joined Yahoo, where I've since then worked on mobile, personalisation and search. My academic background has been very beneficial here, in knowing how to combine tactical studies into a bigger strategic picture.

Moving into industry has been extremely worthwhile, as I gained invaluable experiences working with actual products and end-to-end data collection. The people, resources and data are incredible, and your research has the potential to impact millions of users.

Beyond the sheer concentration of *tech*, a big difference between the Bay Area and the Netherlands is the much higher tolerance for professional risk. Failure isn't seen as the end of the world, it's a learning opportunity (even though you better make sure you learn fast). Ambitions are bigger and resources are much more readily available, both in terms of funding and expert advice. I'd love to see more resources for start-ups and interaction design research in Amsterdam, as it can be a great place to work and especially live." Ω

"Failure isn't seen as the end of the world,.."

→ Insider's advice
"Build a portfolio and a network, and go all in. Rejections happen, they're not the end. Meet as many people as you can and showcase your creativity and skills."

puzzle

Stunning study succes riddle

How can you turn 14 graduated master students into 15?

Answer puzzle issue 1

The answer to the puzzle in issue 1 of Amsterdam Science magazine is

S= 5, I= 9, X= 7,
Y= 3, T= 8, R= 1,
O= 4, and F= 0

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Citizen science tracks bird behaviour: the *Vogel het uit!* project

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Figure
Lesser black-backed gull with UvA-BiTS GPS-logger on board.
© Kees Camphuysen

"Some sites seem to be a 'personal favourite' of a particular gull"

VOGEL HET UIT!
facebook.com/VogelHetUit

Using your smartphone to contribute to scientific research is possible with *Vogel het uit!*, a citizen science project connected to our research on bird behaviour. We use a flexible, high-tech GPS Bird Tracking System – the UvA-BiTS – to tag birds and study their daily movements. This system gives us a wealth of information on where and when birds travel, but not on *why* birds prefer certain locations in the Netherlands. As an interdisciplinary team connected to the University of Amsterdam we therefore developed a communication plan and with it won the 2013 Academic Year Prize organised by NWO, NRC Media, the KNAW and VPRO/NTR. The prize allowed us to create a smartphone app, an accompanying website and social-media outlets where anyone can follow and contribute to our research.

The main goals of the project were to engage the general public in scientific research, to collect information that could help us understand why tagged birds frequent certain locations; and to increase our knowledge of bird behaviour. Through the *Vogel het uit!* app, we collect data for five different bird species. Locations visited by tagged birds for which we need more information about their surrounding environment can be easily found with the app. Our requests to app users vary from taking pictures of potential food sources or specific landscape features (like temporary water bodies) to counting the number of birds present. For example, our tracking data have revealed that certain places in the city and in the countryside are very popular with lesser black-backed and herring gulls. We would like to understand why, considering that both types of gulls are marine species.

Since the launch of *Vogel het uit!* in May 2014, many people have become active participants in scientific research. The information we have received until now is useful for generating more insight into how birds interact with their environment. For example, for gulls visiting Amsterdam from their colony on Texel, app users have sent us pictures of busy locations in the city showing possible food sources. Bird-count data have revealed how some sites, while not attracting a large number of gulls on a regular basis, seem to be personal favourites of particular gulls. Data collection and interpretation is still an ongoing activity, but even now we can definitely conclude that thinking out of the box by placing research in the public arena can yield new insights and increased public participation in science. Ω